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EXAMINER	
JUNG, UNSU	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 11/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/089,233	BIESCHKE ET AL.	
	Examiner	Art Unit	
	Unsu Jung	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20-38* is/are pending in the application.

4a) Of the above claim(s) *38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-37* is/are rejected.

7)☒ Claim(s) *23,27-29 and 32* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 March 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/16/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' preliminary amendments to the specification in the reply filed on September 19, 2002 and preliminary amendments to the drawings in the reply filed on March 6, 2003 have been acknowledged and entered.

Election/Restrictions

2. Applicant's election of species A (claim 31) in the reply filed on September 6, 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. Claims 20-38 are pending, claim 38 is withdrawn from consideration, and claims 20-37 are under consideration for their merits.

Drawings

4. The drawings are objected to because of the following reasons.

- Fig.1 has a number 42 in a circle on the bottom left corner and it is not clear whether or not the number 42 should be part of the figure.
- Description of the inset panel of Fig. 6a) is missing.
- Fig. 12 label on p12/21 is missing.

- Lines of dots and dashes, short dashes, and thin solid line in Fig 15a) as indicated in the specification (p5, last paragraph) are not distinguishable.
- Fig. 16 label on p12/21 is missing and is missing in the list of figures on p6 of the specification.

Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

5. The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they do not include the following reference sign(s) mentioned in the description:

- a) and b) in Fig. 7 (p4, 3rd paragraph); and
- a) and b) in Fig. 21 (p7, 1st paragraph);

Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Specification

6. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

The current abstract is in a bullet form. According to MPEP § 608.01(b), the abstract should be in narrative form and generally limited to a single paragraph.

The current Abstract contains legal phraseology, "said" in line 5, 6, and 9.

7. The use of the trademark ALEXA FLUOR™, OREGON GREEN®, CY2™, CY5™, SEPHADEX®, TWEEN®, FLUOSPHERE®, and FLUOROLINK™, has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

8. Claims 23, 27-29, and 32 are objected to because of the following informalities: the word "effected" should be changed to "affected." Appropriate correction is required.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 20-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

11. Claims 20-37 rejected under 35 U.S.C. 112, second paragraph, as being indefinite in that it fails to point out what is included or excluded by the claim language. This claim is an omnibus type claim.

12. The claims are generally narrative and indefinite, failing to conform with current U.S. practice. They appear to be a literal translation into English from a foreign document and are replete with grammatical and idiomatic errors.

13. Claim 20 is vague and indefinite as it lacks steps for performing the method of the claimed invention.

14. Regarding claim 20, the phrase "especially" renders the claim indefinite because it is unclear whether the limitations “molecules or molecular aggregates” following the phrase are part of the claimed invention. The phrase “especially”, which suggests or makes optional but does not require steps to be performed, does not limit the scope of a claim or claim limitation.

15. In claim 20, the term "especially molecules or molecular aggregates" are vague and indefinite. Further, it is unclear whether or not the term "especially molecules or molecular aggregates" is referring to "the particles" in line 5.

16. Regarding claim 20, the phrase "preferably" renders the claim indefinite because it is unclear whether the limitations "a multitude of binding sites, for at least one of said at least two different detectable probes" following the phrase are part of the claimed invention. The phrase "preferably", which suggests or makes optional but does not require steps to be performed, does not limit the scope of a claim or claim limitation.

17. Claim 20 recites the limitation "the number of bound probes" in line 12. There is insufficient antecedent basis for this limitation in the claim.

18. In claim 20, the term "determining particles" in line 14 is vague and indefinite. The specification does not define the phrase and it is unclear what is meant by the term "determining particles." Further clarification of the term is required. For the purpose of examination, the term "determining particles" has been interpreted as being "mutual ratio of bound probes on the basis of single particle."

19. In claim 21, the term "determining particles" in line 3 is vague and indefinite. It is unclear whether or not the term "determining particles" in line 3 of claim 21 is referring to "determining particles" of claim 20. For the purpose of examination, the term

"determining particles" in line 3 of claim 21 has been interpreted as referring to "determining particles" of claim 20.

20. In claim 23, the term "bound probes" in line 2 is vague and indefinite. It is unclear whether or not the term "bound probes" of claim 23 is referring to "bound probes" of claim 20. For the purpose of examination, the term "bound probes" of claim 23 has been interpreted as referring to "bound probes" of claim 20.

21. Regarding claim 24, the phrase "especially" renders the claim indefinite because it is unclear whether the limitations "measuring volume $\leq 10^{-14}$ l" following the phrase are part of the claimed invention. The phrase "especially", which suggests or makes optional but does not require steps to be performed, does not limit the scope of a claim or claim limitation.

22. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely

exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 24 recites the broad recitation measuring volume $\leq 10^{-12}$ l, and the claim also recites measuring volume $\leq 10^{-14}$ l which is the narrower statement of the range/limitation.

23. In claim 26, the phrase "the determination and characterization of particles is effected in a homogeneous assay method without washing steps" is vague and indefinite. It is unclear how the determination and characterization of particles is effected in a homogeneous assay method without washing steps. Further clarification of the phrase is required.

24. Claim 27 recites the limitation "the quantification" in line 2. There is insufficient antecedent basis for this limitation in the claim.

25. Claim 27 recites the limitation "the particle-cased signal fraction" in lines 2-3. There is insufficient antecedent basis for this limitation in the claim.

26. In claim 27, the phrase "particle-caused signal fraction is preferably effected by analyzing the intensity distribution of a measured detection signal" is vague and

indefinite. It is unclear how the particle-caused signal fraction is effected by analyzing the intensity distribution. Further clarification of the phrase is required.

27. Claim 27 recites the limitation "the intensity distribution" in lines 3-4. There is insufficient antecedent basis for this limitation in the claim.

28. Regarding claim 27, the phrase "especially" renders the claim indefinite because it is unclear whether the limitations “a fluorescence signal” following the phrase are part of the claimed invention. The phrase “especially”, which suggests or makes optional but does not require steps to be performed, does not limit the scope of a claim or claim limitation.

29. Regarding claim 27, the phrase "preferably" renders the claim indefinite because it is unclear whether the limitations “effected by analyzing the intensity distribution of a measured detection signal” following the phrase are part of the claimed invention. The phrase “preferably”, which suggests or makes optional but does not require steps to be performed, does not limit the scope of a claim or claim limitation.

30. Claim 28 recites the limitation "the particle-cased signal fraction" in lines 2-3. There is insufficient antecedent basis for this limitation in the claim.

31. In claim 28, the phrase "particle-caused signal fraction is effected by an algorithm for peak detection and analysis" is vague and indefinite. It is unclear how the particle-caused signal fraction is effected by an algorithm for peak detection and analysis. Further clarification of the phrase is required.

32. Claim 29 recites the limitation "scanning" in lines 3-4. There is insufficient antecedent basis for this limitation in the claim.

33. In claim 29, the phrase "scanning of the sample is effected by producing an essentially constant relative movement between the sample and measuring volume" is vague and indefinite. It is unclear how the scanning of the sample is effected by producing an essentially constant relative movement between the sample and measuring volume. Further clarification of the phrase is required.

34. In claim 31, the term "probe molecules" in line 2 is vague and indefinite. It is unclear whether or not the term "probe molecules" in line 2 of claim 31 is referring to "detectable probes" of claim 20. For the purpose of examination, the term "probe molecules" in line 2 of claim 31 has been interpreted as referring to "detectable probes" of claim 20.

35. In claim 32, the term "probes" in line 2 is vague and indefinite. It is unclear whether or not the term "probes" in line 2 of claim 32 is referring to "detectable probes"

of claim 20. For the purpose of examination, the term “probes” in line 2 of claim 32 has been interpreted as referring to “detectable probes” of claim 20.

36. Regarding claim 32, the phrase "especially" renders the claim indefinite because it is unclear whether the limitations “fluorescent probes, which are separately measurable in the same measuring volume and emitting in different wavelength regions or polarization planes is effected” following the phrase are part of the claimed invention. The phrase “especially”, which suggests or makes optional but does not require steps to be performed, does not limit the scope of a claim or claim limitation.

37. Claim 32 recites the limitation "the same measuring volume" in line 4. There is insufficient antecedent basis for this limitation in the claim.

38. In claim 32, the phrase “emitting in different wavelength regions or polarization planes is effected” is vague and indefinite. It is unclear what is being effected by emitting in different wavelength regions or polarization planes. Further clarification of the phrase is required.

39. Regarding claim 33, the phrase "optionally" renders the claim indefinite because it is unclear whether the limitations “arranged in a multidimensional, especially two-dimensional, array for evaluation, for example, arranged as an intensity histogram” following the phrase are part of the claimed invention. The phrase “optionally”, which

suggests or makes optional but does not require steps to be performed, does not limit the scope of a claim or claim limitation.

40. Regarding claim 33, the phrase "especially" renders the claim indefinite because it is unclear whether the limitations "two-dimensional, array for evaluation, for example, arranged as an intensity histogram" following the phrase are part of the claimed invention. The phrase "especially", which suggests or makes optional but does not require steps to be performed, does not limit the scope of a claim or claim limitation.

41. Regarding claim 33, the phrase "for example" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

42. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required

feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 33 recites the broad recitation multidimensional array, the claim also recites two-dimensional array, which is the narrower statement of the range/limitation, and the claim further recites an intensity histogram, which is even narrower statement of the range/limitation.

43. Regarding claim 34, the phrase "especially" renders the claim indefinite because it is unclear whether the limitations "prion proteins by subspecies" following the phrase are part of the claimed invention. The phrase "especially", which suggests or makes optional but does not require steps to be performed, does not limit the scope of a claim or claim limitation.

44. In claim 34, the term "prion proteins by subspecies" in line 2 are vague and indefinite. It is unclear how the term "prion proteins by subspecies" are related to "particles" in line 3.

45. In claim 34, the term "particles" in line 3 is vague and indefinite. It is unclear whether or not the term "particles" in line 3 of claim 34 is referring to "particles" of claim 20. For the purpose of examination, the term "particles" in line 3 of claim 34 has been interpreted as referring to "particles" of claim 20.

46. In claim 34, the term "them" in line 4 is vague and indefinite. It is unclear whether or not the term "them" in line 4 of claim 34 is referring to "aggregates", "particles", "prion proteins", or "subspecies" in claim 34. For the purpose of examination, the term "them" in line 4 of claim 34 has been interpreted as referring to "particles."

47. In claim 35, the term "probe molecules" in line 2 is vague and indefinite. It is unclear whether or not the term "probe molecules" in line 2 of claim 35 is referring to "detectable probes" of claim 20. For the purpose of examination, the term "probe molecules" in line 2 of claim 35 has been interpreted as referring to "detectable probes" of claim 20.

48. In claim 35, the term "the mutual ratio of amounts of different bound probe molecules" in lines 5-6 is vague and indefinite. It is unclear whether or not the term "the mutual ratio of amounts of different bound probe molecules" of claim 35 is referring to "the mutual ratio of bound probes" of claim 20. For the purpose of examination, the term "the mutual ratio of amounts of different bound probe molecules" of claim 35 has been interpreted as referring to "the mutual ratio of bound probes" of claim 20.

49. Claim 36 is vague and indefinite as it is unclear how the method of claim 20 is related to "pathogenic strain typing or examining the relative binding of proteins from different species to pathological protein aggregates of a particular species for estimating

an interspecific barrier for the transmission of a disease." Further clarification is required.

50. Claim 36 recites the limitation "the transmission" in line 5. There is insufficient antecedent basis for this limitation in the claim.

51. In claim 36, the terms "relative binding of the proteins" in line 2 and "pathological protein aggregates" in lines 3-4 are vague and indefinite. It is unclear how the term "relative binding of the proteins" is related to the method of claim 20.

52. Claim 37 is vague and indefinite as it is unclear how the method of claim 20 is related to "examination of degenerative diseases, especially neurodegenerative diseases, with formation of pathological aggregates, especially aggregates which contain prion protein, APP, Tau, synuclein or proteins having a polyglutamine sequence, such as huntingtin, or fragments or derivative of such proteins as a component." Further clarification is required.

53. Regarding claim 37, the phrase "especially" renders the claim indefinite because it is unclear whether the limitations "neurodegenerative diseases" and "aggregates which contain prion protein, APP, Tau, synuclein or proteins having a polyglutamine sequence, such as huntingtin, or fragments or derivative of such proteins as a component" following the phrase are part of the claimed invention. The phrase

"especially", which suggests or makes optional but does not require steps to be performed, does not limit the scope of a claim or claim limitation.

54. In claim 37, the phrase "with formation of pathological aggregates" in line 3 is vague and indefinite. It is unclear whether or not the phrase "with formation of pathological aggregates" is referring to "degenerative diseases" or "neurodegenerative diseases." For the purpose of examination, the phrase "with formation of pathological aggregates" has been interpreted as referring to "neurodegenerative diseases."

Claim Rejections - 35 USC § 102

55. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

56. Claims 20-23, 25-28, 31-35, and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Riesner et al. (U.S. Patent No. 6,498,017, Published as a WO99/15903 document on Apr. 1, 1999).

Riesner et al. anticipates instant claims by teaching a method for determination of individual characterization of particles by means of at least two different detectable probes in a sample, wherein the particles, which are molecules or molecular aggregates, have at least one binding site for at least one of said detectable probes

(column 4, lines 51-60). The two different detectable probes are present in the sample and the number of bound probes is measured (column 6, lines 5-13) and the mutual ratio of bound probes is established on the basis of a single particle (column 8, lines 1-4 and column 11, lines 26-37).

With respect to claim 22, Riesner et al. teaches a method, wherein the determination is on the basis of the single particle, which are within the measuring volume at different times (Fig. 2).

With respect to claim 25, Riesner et al. teaches a method, wherein the measurement is performed using a confocal microscopic set-up (column 4, lines 28-31).

With respect to claim 26, Riesner et al. teaches a method, wherein the determination and characterization of the particles performed in a homogeneous assay method without washing steps (column 11, lines 26-37).

With respect to claim 28, Riesner et al. teaches a method, wherein an intensity-based separation of the particle-caused signal fraction is effected by an algorithm for peak detection and analysis (column 8, lines 39-42).

With respect to claim 31, Riesner et al. teaches a method, wherein the probes are antibodies (column 4, lines 25-27).

With respect to claim 32, Riesner et al. teaches a method, wherein simultaneous analysis of two or more probes are separately measurable in the same measuring volume and emitting in different wavelength regions (column 11, lines 26-37).

With respect to claim 33, Riesner et al. teaches a method, wherein the data from dual color measurements are established (column 11, lines 26-37).

With respect to claim 34, Riesner et al. teaches a method, wherein the pathological protein (prion proteins) aggregates are detected (column 11, lines 26-37).

With respect to claim 37, Riesner et al. teaches a method, wherein the method is used for examination of neurodegenerative diseases (column 14, lines 13-15).

Claim Rejections - 35 USC § 103

57. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

58. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

59. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

60. Claims 24, 29, and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Riesner et al. (U.S. Patent No. 6,498,017, Published as a WO99/15903 document on Apr. 1, 1999) in view of Günther (U.S. Patent No. 5,933,233, Aug. 3, 1999).

Riesner et al. teaches a method for determination of individual characterization of particles by means of at least two different detectable probes in a sample as discussed above. Riesner et al. further teaches that fluorescence correlation spectroscopy (FCS) as described in WO 96/13744 can be employed to detect properties of particles (column 4, lines 28-35). However, Riesner et al. fails to specifically teach a method, wherein the measuring volume is $\leq 10^{-12}$ l and the scanning of the sample is effected by producing an essentially constant relative movement between the sample and measuring volume by a lens system, which allows for movement of the measuring volume by a flow capillary.

Günther teaches a FCS, which uses a measuring volume of $<<10^{-12}$ l (column 5, lines 54-56), and a flow capillary, which allows for movement of the measuring volume, which includes sample (column 3, lines 62-67).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to employ the FCS system of Günther in the method of Riesner et al. in order to determine/characterize fluorescent properties of particles present in a sample as Riesner et al. teaches that FCS of Günther (WO 96/13744) can be employed to detect properties of particles.

61. Claim 36 is rejected under 35 U.S.C. 103(a) as being unpatentable over Riesner et al. (U.S. Patent No. 6,498,017, Published as a WO99/15903 document on Apr. 1, 1999) in view of Prusiner (U.S. Patent No. 6,020,537, Filed on Nov. 25, 1998).

Riesner et al. teaches a method for determination of individual characterization of particles by means of at least two different detectable probes in a sample as discussed above. However, Riesner et al. fails to teach a method, wherein the method is used for pathogenic strain typing or for examining the relative binding of proteins from different species to pathological protein aggregates of a particular species for estimating an interspecific barrier for the transmission of a disease.

Prusiner teaches a method of providing a multiprion standard, in which multiple samples of prions of different variants and/or species are discretely distributed in a single standard, allowing the identification of the particular sample that reacts with an agent (column 20, lines 1-13). Antibodies that recognize a conserved epitope on all the species of prions and antibodies that recognize each species can be used to detect particular sample that reacts with the prions of different species for determination of different samples that will infect different species of prions (column 19, lines 50-67).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to employ the multiprion standard and antibodies of Prusiner in the method of Riesner et al. in order to determine different samples that will infect different species of prions (examining the relative binding of proteins from different species to pathological protein aggregates of a particular species for estimating an interspecific barrier for the transmission of a disease). The advantage of using a standard comprising multiple species of prions provides the motivation to combine teachings of Riesner et al. and Prusiner with a reasonable expectation of success as multiprion standard can be used to determine different samples that will infect different species of prions contained in the multiprion standard.

Prior Art of Record

62. The following prior art made of record and not relied upon are considered pertinent to applicant's disclosure.

- Bieschke et al. (PNAS, May 9, 2000, Vol. 97, pp5468-5473) teaches a method of detecting pathological prion protein aggregates labeled with fluorescent markers using dual-color scanning (entire document);
- Eigen et al. (U.S. Patent No. 6,200,818, Mar. 13, 2001) teaches a method for detecting reactions of analytes in a sample by coincidence analysis (entire document); and
- Pitschke et al. (Nature Medicine, 1998, Vol. 4, pp832-834) teaches a method of detecting single amyloid β-protein aggregates in the

cerebrospinal fluid of Alzheimer's patients using FCS (entire document).

Conclusion

63. No claim is allowed.

64. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Unsu Jung whose telephone number is 571-272-8506. The examiner can normally be reached on M-F: 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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